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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,292	07/03/2001	Michele Amouyal	1231-01	2241

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EXAMINER	
CALAMITA, HEATHER	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/22/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/898,292	AMOUYAL, MICHELE	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-14,16-18,20-23 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14,16-18,20-23 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 04, 2006, has been entered.

Status of Application, Amendments, and/or Claims

2. Claims 11-14, 16-18, 20-23 and 28 are pending and under examination. All arguments have been fully considered and thoroughly reviewed, but are deemed not persuasive for the reasons that follow. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Interpretation

3. Claim 11 is amended to include the limitation "wherein said DNA compaction agent is present at a concentration sufficient to allow the DNA insert to remain flexible." This is read as any concentration that will permit the ligation reaction to occur.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-14, 16-18, 22, 23 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hodgson et al. (USPN 6,410,220 B1 06/25/2002).

Hodgson et al. teach (claims 11 and 28) a method for preparing circularized recombinant nucleic acids from a vector and an insert by ligating a DNA insert and a DNA vector in the presence of a DNA compaction agent selected from the group consisting of histone proteins, histone protein derivatives, viral envelope proteins, bacterial chromoid proteins, non-histone chromosomal proteins, HMGs derivatives of said proteins, and mixtures of said proteins and protein derivatives and selecting said circularized recombinant nucleic acid

wherein said DNA compaction agent is present at a concentration sufficient to allow the DNA insert to remain flexible and wherein said circularized recombinant nucleic acid is greater than 5kb (see col. 23 lines 17-27 and lines 22-24).

With regard to claims 12 and 27, Hodgson et al. teach the circularized recombinant nucleic acid as greater than 10 kb (see col. 23 lines 22-24).

With regard to claim 13, Hodgson et al. teach the selection steps of transferring the circularized recombinant nucleic acid into a cellular medium, cloning nucleic acid, and testing for the presence of the insert in the circularized recombinant nucleic acid (see col. 23 lines 22-27).

With regard to claim 14, Hodgson et al. teach the DNA compaction agent is selected from the group consisting of a protein, a mixture of proteins and protein derivatives exhibiting the properties of the DNA compaction agent (see col. 23 lines 49-51).

With regard to claims 16, 17, 18, Hodgson et al. teach adding a ligase to a ligation medium containing the DNA in solution in ligation buffer or adding the compaction agent to the ligation medium prior to the addition of ligase or adding the ligase and the compaction agent simultaneously (see col. 23 line 52).

With regard to claim 22, Hodgson et al. teach the ligation medium comprising a stabilizing agent that prevents denaturation, aggregation, and absorption of the DNA compaction agent (see col. 23 line 52).

With regard to claim 23, Hodgson et al. teach histone proteins (see col. 23 line 51).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hodgson et al. (USPN 6,410,220 B1 06/25/2002) in view of Nagaki et al. (*BBRC* 246:137-141, 1998).

The teachings of Hodgson et al. are described previously.

Hodgson et al. do not teach a specific amount of HMG to use in the ligation reaction.

Nagaki et al. do teach using a range of 0.5 μg to 2.0 μg of HMG in the ligation reaction (see Fig. 2, page 139).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Nagaki's method of using a range of HMG concentrations with Hodgson's method of ligating insert and vector DNA in order to determine the amount of protein needed for the reaction. Nagaki et al. teach that HMG1 and HMG2 stimulate cohesive-end and blunt-end ligations with DNA ligase (see col. 2 2nd paragraph pp 137-138). It would have been prima facie obvious to apply Nagaki's range of HMG

concentrations with Hodgson's method for ligating insert and vector DNA to achieve the expected advantage of achieving optimal ligation activity with a given amount of DNA and HMG.

Response to Arguments

6. Applicant's arguments filed December 4, 2006, have been fully considered and are not found persuasive.

Applicant argues Hodgson describes the use of histones and other compacting agents along with transfection agents as a method of reducing shearing when transferring already ligated DNA constructs to the cells to be transfected and that one skilled in the art would appreciate that a DNA molecule which is prepared for transfection into a cell as described in Hodgson has been completely ligated and thus Hodgson describes adding the compacting agents after ligation has taken place and the instant claims are drawn to the addition of condensing agent prior to the ligation reaction. This argument is not persuasive because Applicant mischaracterizes the teachings of Hodgson. Hodgson teaches the addition of condensing reagent directly to the DNA ligation reaction at col. 23 lines 49-52 states, "Another method is to add a DNA condensing reagent (dendrimers, polycations [such as polyethyleneamine] histones or liposomes) directly to the DNA ligation reaction." It is clear that the condensing agent is added directly to the ligation reaction. Typically a ligation reaction contains a vector, insert, ligase, buffer and in this instance a condensing agent. Hodgson does not disclose that the ligation reaction is completed prior to the addition of condensing reagent.

Additionally, Applicant argues Hodgson et al. do not anticipate the instant claims because Hodgson does not disclose a concentration of compacting agent which allows enough flexibility for the linear DNA to form circular constructs. This argument is not persuasive because DNA condensed on a histone protein is not rigid there is no evidence the DNA insert of Hodgson does not retain flexibility. The ligation reaction of Hodgson yields a functional construct, therefore there is no evidence that the

concentration of compaction agent added by Hodgson is at a concentration other than one sufficient to allow the DNA insert to remain flexible. Presumably if the concentration of compaction agent used by Hodgson resulted in rigidity of the DNA insert, the ligation reaction would be impeded because the DNA would be unable to bend and there would not be any contact between the ends of the finished vector and ligation would not occur, however again Hodgson discloses a working construct which necessitates ligation occur meaning the DNA insert was not too rigid as to impede the ligation reaction.

Applicants argue the Office Action asserts that the rigidity of condensed DNA was not well known in the art at the time the application was filed. This Office Action is mischaracterized. The Office Action does not assert that rigidity of DNA was not well known but rather asserts on p. 5

> binding of any substance to a DNA molecule will necessarily reduce the molecule's flexibility to some degree and asstated above, if the concentration of compaction agent used by Hodgson resulted in rigidity of the DNA insert, the ligation reaction would be impeded because the DNA would be unable to bend and there would not be any contact between the ends of the finished vector and ligation would not occur, however Hodgson discloses a working construct which necessitates ligation occur meaning the DNA insert was not too rigid as to impede the ligation reaction, therefore the compaction agent of Hodgson is necessarily present in a concentration sufficient to allow the DNA insert to remain flexible.

The rejections over Hodgson are therefore maintained.

With respect to the 103 (a) rejection, Applicant argues Nagaki discloses a process of making linearized dimmers and the use of HMG proteins does not lead to circularized molecules. This argument is not persuasive to overcome the 103 (a) rejections of claims 20 and 21 because Nagaki is not relied on for the teaching of ligating circularized molecules. Nagaki is relied on for the teaching of a specific amount of compaction agent to be used in a ligation reaction. As discussed above Nagaki teach using a range of 0.5 μg to 2.0 μg of HMG in the ligation reaction (see Fig. 2, page 139) which meets the concentration limitations recited in claims 20 and 21. Additionally, Nagaki et al. clearly disclose a ligation reaction in the presence of condensing reagent (see p. 139 Figure 2 and legend) and further

disclose the presence of HMG 1 and HMG 2 at particular concentrations enhanced the ligation reactions (see p. 140 1st sentence under Discussion).

Applicant argues any experimental methods disclosed in Nagaki are irrelevant to the method as recited in claims 21 and 22. This argument is not persuasive because a skilled artisan wanting to improve ligation efficiency would, after reading the teachings of Nagaki, be motivated to use condensing agents in a ligation reaction because Nagaki clearly teach the addition of such condensing agents at the specifc amounts of 0.5 μg to 2.0 μg improves ligation efficiency. The 103 (a) rejections are therefore maintained.

Summary

7. No claims were allowable.

Conclusion

8. This is a continuation of prosecution of applicant's earlier Application No. 09898292. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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